IN VIVO CAR-T CELL THERAPY: SCIENCE & TECHNOLOGY

NEWS: Technique to make CAR T-cells in vivo could transform cancer care

WHAT'S IN THE NEWS?

Researchers have developed an in vivo CAR-T cell therapy that programs immune cells inside the body using mRNA and lipid nanoparticles, offering a safer, cheaper alternative to lab-based CAR-T cell generation, though human trials are pending.

In vivo CAR-T Cell Therapy: A Breakthrough Approach

- Researchers have developed an innovative method of generating CAR-T cells directly inside the patient's body using messenger RNA (mRNA) and lipid nanoparticles (LNPs).
- This method eliminates the need for conventional lab-based manipulation, which typically involves extracting, modifying, and expanding T-cells outside the body before reinfusing them into the patient.

How In vivo CAR T-cell Generation Works

- Scientists engineered LNPs carrying mRNA instructions that encode chimeric antigen receptors (CARs).
- These LNPs are specifically targeted to CD8+ cytotoxic T cells using antibodies that bind to the CD8 receptor on T-cell membranes.
- Once infused into the bloodstream, the T-cells absorb the LNP-delivered mRNA and temporarily express the CARs.
- These engineered CAR-T cells then circulate to identify and destroy target B-cells expressing specific markers such as CD19+ or CD20+, commonly found in B-cell cancers.

What is CAR-T Cell Therapy?

- CAR-T therapy is a form of advanced immunotherapy in which a patient's T-cells are genetically modified to target specific cancer cells.
- T-cells, particularly cytotoxic CD8+ cells, play a crucial role in the immune system by eliminating virus-infected, abnormal, or malignant cells.
- Conventional CAR-T cell therapy involves:
    - Extraction of T-cells from a patient's blood.
    - Genetic modification of T-cells in the laboratory to express CARs that specifically bind to cancer cell surface antigens.
    - Expansion of these modified CAR-T cells.
    - Infusion of the engineered cells back into the patient, where they seek out and destroy cancerous B-cells.

Why CAR-T Cell Therapy is Effective

- Generates immunogenic memory, allowing continuous surveillance to target local or distant cancerous lesions.
- Reduces dependence on aggressive chemotherapy and bone marrow transplantation.
- Provides potent, targeted immune responses against specific cancer cell markers, reducing collateral damage to healthy cells.
- Clinical success: Studies show up to 90% complete remission rates in patients with difficult-to-treat acute lymphoblastic leukemia.
- Cost factor: Indigenous CAR-T therapy in India reduces costs from ₹4 crore to approximately ₹40 lakh.

Significance of In vivo CAR-T Cell Therapy

- Conventional CAR-T therapy in India can cost ₹60–70 lakh, with nearly half of the cost attributed to cell processing in specialized labs.
- The in vivo method requires no specialized manufacturing, significantly lowering costs and logistical barriers.
- It avoids the need for chemotherapy-based lymphodepletion — reducing infection risks and shortening hospital stays, making it safer for elderly, frail, or comorbid patients.
- Particularly relevant for India, where B-cell driven cancers such as:
    - Diffuse large B-cell lymphoma (which constitutes 34–60% of non-Hodgkin lymphoma cases).
    - Acute lymphoblastic leukemia (accounting for 75% of childhood cancers).

Limitations and Future Prospects

- This approach is currently in preclinical stages with ongoing animal studies — human trials are yet to begin.
- Further research is needed to establish long-term safety, durability of CAR expression, and potential side effects.

Conclusion

- In vivo CAR-T therapy represents a promising leap in cancer treatment, potentially democratizing access to advanced immunotherapies by reducing costs, complexity, and treatment risks — especially important for countries like India with high incidence of B-cell malignancies.

Source: https://www.thehindu.com/sci-tech/science/technique-to-make-car-t-cells-in-vivo-could-transform-cancer-care/article69714559.ece